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At the time this paper was written, David W. Fraser and Roger A. Feldman were members of the staff of the Center for Disease Control, U.S. Public Health Service, Atlanta, Georgia. James E. Mitchell was on the staff of the Vermont State Department of Health; and Lester P. Silverman was a member of the staff of the Public Research Institute, Center for Naval Analyses, Arlington, Virginia. This paper represents the opinion of the authors. It does not necessarily represent the opinion of the institutions of which they were members.

ABSTRACT

Community-acquired bacterial meningitis in Vermont children under 5 years of age was recognized less frequently in 1967-1970 in those towns with low total hospitalization rates than in towns with hospitalization rates above 15 admissions per 100 population. Using the towns with high hospitalization rates as a norm, it was found that towns with fewer recognized meningitis cases than expected had significantly greater rates of death from obscure causes in children 1-59 months of age in 1967-1970. It is suggested that about 17 deaths in 1967-1970 in Vermont children 1-59 months of age were associated with the failure to recognize bacterial meningitis in children from towns with low rates of medical care utilization.

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As part of a study of risk factors in bacterial meningitis (1-3) we examined rates of bacterial meningitis in Vermont residents in 1967-1970. We found evidence that in those towns where hospitalization rates were relatively low, rates of recognized bacterial meningitis in children were low, and death rates in children from vaguely defined illnesses were high when compared to towns with higher hospitalization rates. This study suggests that a significant number of cases of bacterial meningitis in children went undiagnosed in Vermont towns that had low rates of medical care utilization.

MATERIALS AND METHODS

Case Finding

Cases of bacterial meningitis and of acute meningitis of unknown cause in Vermont residents with onset in 1967-1970 were sought by review of 1) hospital records of each of Vermont's 19 acute care hospitals and of the Mary Hitchcock Hospital, Hanover, New Hampshire; 2) death certificates; 3) cases of meningitis reported to the State Department of Health. Those hospital records coded under the following categories were reviewed: bacterial meningitis, meningococcal disease, listeriosis, tuberculous disease of the brain and meninges, aseptic meningitis, acute poliomyelitis, and encephalitis. In addition, the records of the 16 acute care hospitals in the Eastern Townships, Quebec -- the area bordering Vermont -- and those of the Elliot Community Hospital, Keene, New Hampshire, were searched for cases of bacterial meningitis or meningococcal disease in Vermont residents discharged in 1967-1970 (L. Munan and G. L. Fuld, personal communications).

A case was considered bacterial meningitis if a pathogenic organism (i.e., other than Staphylococcus epidermidis, alpha-hemolytic streptococcus, or a diphtheroid) was isolated from cerebrospinal fluid or if postmortem examination demonstrated purulent meningitis. A case was considered acute meningitis of unknown cause if it did not meet the criteria for bacterial meningitis but if the initial CSF specimen examined contained 100 or more white blood cells per cubic mm and either a majority of polymorphonuclears or a glucose concentration less than 30 mg per 100 ml. Excluded from both groups were patients with a history of a neurosurgical procedure invading the subarachnoid space in the preceding 6 months or with an indwelling neurosurgical device.

Town Information

The basic unit of analysis for this study was the town. Data on demographic characteristics of the 255 towns, of which 247 were populated in 1970, were taken from the 1970 decennial census. The variables analyzed in this study and their mean values and standard deviations across towns are shown in table 1. The number of deaths in 1967-1970 in Vermont children 1 to 59 months of age, by stated cause and town, was obtained from death certificates provided by the State Department of Health. Information of physician location by specialty was taken from the audited records of the State Department

TABLE 1

MEAN VALUES AND STANDARD DEVIATIONS OF 12 DEMOGRAPHIC AND HEALTH CARE VARIABLES USED IN ANALYSIS OF MENINGITIS RATES

Variable	Mean	Standard Deviation
Town population	1797.449	3416.21
Percent of population under 5 years of age	9.558	8.05
Population per square mile	95.381	341.54
Persons per household	3.339	.33
Percent of families in residences with less than .75 persons per room	70.960	18.44
Percent of families with income under .75 of poverty level	6.761	7.16
Deaths from all causes in children 1 to 59 months of age per 100,000 population per year	147.518	351.48
General practitioner or internist, or neither, in town (1 = one or both, 0 = neither)	.287	.45
Pediatrician, or not, in town (1 = yes, 0 = no)	.053	.22
Osteopath, or not, in town (1 = yes, 0 = no)	.081	.27
Other medical specialist, or not, in town (1 = yes, 0 = no)	.113	32
Hospital admissions of town residents in 1969/ total population	.123	.07

of Health. The number of hospital admissions of town residents in 1969 to all acute care hospitals in Vermont (except the Veterans Administration Hospital) and to the Mary Hitchcock Hospital, Hanover, New Hampshire, and the Albany Medical Center, Albany, New York, was provided by Dr. J. Wennberg formerly of the Northern New England Regional Medical Program.

Statistical Methods

To estimate the separate effects of individual variables on the rates of meningitis, we used a procedure developed by Tobin (4) that is a hybrid between probit analysis (which seeks to predict whether a town will have any cases) and multiple regression (which estimates the expected number of cases given that there is at least one). This method allows analysis of data in which a substantial proportion of the towns have no cases.

In the equation

$$y = b_o + b_1 X_1 + \ldots + b_n X_n$$

where y is the dependent variable (meningitis rate) and X_i is one of several independent variables (e.g., population, persons per household, etc.), the marginal effect of an extra unit of X_i on y holding all other factors constant is b_i. To compare the magnitude of effects of independent variables of differing scales on the meningitis rate, we used a unitless measure, the elasticity:

$$\text{elasticity of } X_i = b_i \quad \frac{\mu_{X_i}}{\mu_y}$$

where μ_{X_i} is the mean value of X_i over the observations (towns) in the sample and μ_y is the mean value of the dependent variable. The elasticity expresses the percentage change in the dependent variable that can be expected from a one percent change (at the mean) of that independent variable, holding all other independent variables constant.

RESULTS

In Vermont residents, 145 cases of bacterial meningitis and 68 cases of acute meningitis of unknown cause with onset in 1967-1970 were identified. The incidence rates of bacterial meningitis by age and by organism are shown in table 2. A total of 94 cases of proven bacterial meningitis and 32 cases of acute meningitis of unknown cause were in children under 5 years of age. Of the nine neonates who developed cases of bacterial meningitis, none left the hospital between birth and the onset of meningitis. These 9 nosocomial cases are excluded from the subsequent analysis of town of residence.

TABLE 2

CASES OF BACTERIAL MENINGITIS BY AGE
AND ORGANISM IN VERMONT RESIDENTS, 1967-1970

Organism	Age			Total	Incidence rate +
	< 1 month	1-59 months	≥ 5 years		
Hemophilus influenzae	0	55	5	60	3.4
Neisseria meningitidis	0	16	13	29	1.6
Streptococcus pneumoniae	0	5	24	29	1.6
Other*	9	9	9	27	1.5
Total	9	85	51	145	8.2

*Escherichia coli - 7, Staphylococcus aureus - 4, H. parainfluenzae - 2, Paracolon sp. - 2, Streptococcus sp. - 2 (group A-1, β - hemolytic - 1), Flavobacterium meningosepticum - 1, Listeria monocytogenes - 1, Mycobacterium tuberculosis - 1, Salmonella sp. - 1, coliform bacillus - 1, N. meningitidis + H. influenzae - 1, N. meningitidis + S. pneumoniae - 1, N. meningitidis + S. pyogenes - 1, unknown bacteria - 1.

+Cases per 100,000 population per year (all ages)

Table 3 contains the elasticities of the 12 independent variables in table 1 in the equations predicting the incidence rates of bacterial meningitis and of acute meningitis of unknown cause in children under 5 years of age and in persons 5 years of age and older. In children under 5 years of age, rates of diagnosed bacterial meningitis were significantly higher in towns with higher rates of hospitalization in 1969 of persons of all age groups ($p<.05$); as table 3 shows, a one percent increase in hospital admission rate (from .123 to .124 admissions per person) was associated with a 3.43 percent increase in the incidence of community acquired meningitis in children under 5 years of age (from 36.2 to 37.4 cases per 100,000 population per year). A similar relation was seen between rates of hospitalization and the incidence rate of acute meningitis of unknown cause in children under 5 years of age, but for that category the presence of a general practitioner or internist in the town was also associated with significantly higher rates of meningitis ($p<.01$). Bacterial meningitis in persons 5 years of age and older was diagnosed more commonly in towns with a general practitioner or internist ($p<.01$) and in towns with a higher proportion of poor persons ($p<.05$). Acute meningitis of unknown cause in persons 5 years of age and older was diagnosed more commonly in towns with a general practitioner or internist than in towns with neither ($p<.05$). Analysis of the effect of the 12 independent variables on the incidence rates of bacterial meningitis was made separately for meningitis caused by different organisms (H. influenzae, S. pneumoniae, N. meningitidis, other) in children under 5 years of age but no clear difference between the different causes of meningitis was found (data not shown).

We added the incidence rate of acute meningitis of unknown cause as a thirteenth variable in the equation estimating the incidence rate of bacterial meningitis. For children under 5 years of age, the effect was not statistically significant. For those over 5 years of age, higher rates of acute meningitis of unknown cause were associated with significantly higher rates of bacterial meningitis ($p<.05$); elasticity = 0.5).

To test if towns with low hospitalization rates had low rates of bacterial meningitis in children under 5 years of age because the diagnoses had been overlooked, we sought to determine whether or not these towns had an excess of deaths in children of this age as might be expected if cases of bacterial meningitis were not identified and properly treated. To do this we first considered separately those 80 Vermont towns that had hospitalization rates above 15 admissions per 100 population in 1969. For these towns only, we estimated the coefficients of the variables in table 1 (excluding the hospitalization rate and four physician availability measures) in predicting the incidence rate of bacterial meningitis in children less than 5 years of age. The underlying assumption was that all cases of bacterial meningitis in those towns would have been detected. The coefficients were then used to predict an expected underlying incidence of bacterial meningitis in children under 5 years of age in each of the 247 towns in 1967-1970. Subtracting the number of cases of documented bacterial meningitis for each town from the expected

TABLE 3

ELASTICITIES OF VARIABLES IN EQUATIONS PREDICTING RATES OF COMMUNITY ACQUIRED BACTERIAL MENINGITIS AND ACUTE MENINGITIS OF UNKNOWN CAUSE IN TOWN RESIDENTS UNDER AND OVER 5 YEARS OF AGE ‡

	Bacterial meningitis		Acute meningitis of unknown cause	
	<5 yrs.	≥5 yrs.	<5 yrs.	≥5 yrs.
Town population	0.49	0.31	- 0.24	2.90
% population < 5 years	-0.20	0.45	-20.62	0.62
Population/sq. mile	0.05	0.34	0.29	-0.21
Persons/household	6.49	13.58	86.85	44.71
% uncrowded families	9.80	11.13	23.06	0.98
% poor families	-0.35	2.98*	-10.75	1.28
Total death rate 1-59 months	0.49	-1.72	- 5.71	-1.96
G.P. or internist, or neither	0.77	2.82+	6.15+	3.68*
Pediatrician, or not	-0.01	0.05	0.48	-0.26
Osteopath, or not	0.28	-0.41	0.35	0.24
Specialist, or not	0.05	0.86	0.12	0.09
Hospital admission rate	3.43*	3.02	13.07*	5.37
Average annual incidence per 100,000 (across towns)	36.2	2.4	19.4	1.4

*$p < .05$

+$p < .01$

‡ The standard goodness of fit measure is not applicable to the Tobin procedure (4) and therefore it is not reported.

incidence showed that 26 towns had a total of 57.8 fewer cases of bacterial meningitis in 1967-1970 in children under 5 years of age than would have been expected from the meningitis rates in towns with high hospitalization rates.

Of the 223 deaths in 1967-1970 in Vermont children 1 to 59 months of age, 10 were caused by recognized bacterial meningitis and an additional 85 were listed on the death certificate as caused by CNS infection, ill-defined CNS or respiratory disease, or ill-defined cause. Some of this latter group of 85 deaths we considered might have been due to unrecognized bacterial meningitis. To test this hypothesis, we included the difference between the expected and observed rates of bacterial meningitis for those towns that had fewer than the expected number of cases with the other variables in table 1 (except the total death rate 1-59 months) in an analysis of the rate of death from uncertain cause (of which there are 85 total) by town using the method of Tobin (7). Towns with fewer cases of bacterial meningitis than expected had significantly higher rates of these deaths in children 1 to 59 months of age than did other towns ($p<.01$), with the other medical and demographic variables in table 1 held constant. It could be predicted from the estimated coefficients in the analysis that, if no town had had fewer cases of bacterial meningitis than were expected, the number of deaths listed as caused by CNS infection (other than bacterial meningitis), ill-defined CNS or respiratory disease, or ill-defined cause in children 1 to 59 months of age would have been 61.4 instead of 85 in 1967-1970. These 23.6 deaths represented 10.6 percent of all deaths in 1967-1970 in children 1 to 59 months of age.

DISCUSSION

Bacterial meningitis was documented more frequently in children under 5 years of age in Vermont towns that had higher hospitalization rates. That observation must be interpreted carefully because variations in the incidence rates of meningitis from town to town may result from differences in underlying risk, completeness of case recognition, completeness of case retrieval, and/or chance variation. In this study, case retrieval appears to have been nearly complete and therefore it probably was not an important cause of variation. Of the 33 fatal cases of bacterial meningitis listed as such on death certificates, only 5 were located solely because death certificates were used as a case finding tool. This suggests that, at least for fatal cases, hospital cross-index chart retrieval was about 85% complete. Surveys of hospitals in New Hampshire and Quebec suggested that few Vermont residents received medical care for meningitis out-of-state. The distribution of cases by county did not suggest that there was a major geographic factor influencing case retrieval, since rates were similar from county to county (data not shown).

If bacterial meningitis had been documented more frequently in towns with higher hospitalization rates because of different sensitivities of bacteriologic technique, acute meningitis of unknown cause would be expected to have been significantly more frequent in towns with lower rates of bacterial meningitis. Conversely, where bacterial meningitis had been frequently documented, acute meningitis of unknown cause would be expected to have been relatively uncommon. Such was not the case, which suggests that inadequacies in bacteriologic technique were not the primary cause of the observed variations from town to town in the incidence rates of bacterial meningitis.

Because untreated or improperly treated cases of bacterial meningitis would be expected to have a high case fatality ratio, towns with unusually low rates of documented bacterial meningitis should have had inflated death rates if low meningitis rates had been due to omission of a significant number of cases that went undiagnosed. The observation that the Vermont towns with fewer cases of bacterial meningitis than expected had significantly more deaths listed as caused by illnesses potentially confusable with bacterial meningitis strengthens this possibility. It is impossible retrospectively to be certain that the association observed between low meningitis rates and high death rates in certain towns reflects a causal relationship, but some circumstantial evidence suggest that this might be true. The projected case fatality ratio among the "undiagnosed" cases of 41 percent (23.6 deaths in 57.8 cases) is considerably higher than the 12 percent (10 deaths in 85 cases) seen in recognized bacterial meningitis in children 1 to 59 months of age but is believable in light of the observation that bacterial meningitis that in the past was essentially untreated had a case fatality ratio of 80 percent or more (5-7).

A deficit in numbers of cases of acute meningitis of unknown cause in children under 5 years of age was seen also in towns with low hospitalization rates. Another index of inferior medical care availability and utilization -- the absence of a general practitioner or internist in the town -- was associated with low rates of acute meningitis of unknown cause in all age groups and of bacterial meningitis in persons 5 years of age and older.

All of these observations are consistent with the thesis that inadequacies in medical care availability and utilization in some Vermont towns were associated with underdiagnosis of meningitis. In children 1 to 59 months of age this may have resulted in about 23 more deaths from bacterial meningitis in 1967-1970 than had been recognized at the time of illness. Because of the difference in case fatality ratios of recognized (12 percent) and unrecognized (41 percent) cases, about 17 of these deaths (.29 x 57.8) might have been prevented if the bacterial meningitis had been recognized at the time of illness.

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